

**REMARKS****I. INTRODUCTION**

Upon entry of the present amendment, claims 1-22 will remain pending in this application. Applicants have amended claim 19 to clarify the scope of the invention. No new matter has been added.

**II. 35 U.S.C. § 112, FIRST PARAGRAPH**

The Examiner has rejected claims 19-22 under 35 U.S.C. § 112, first paragraph, stating that while the specification is enabling for the treatment of tumors, it does not reasonably provide enablement for the prevention of tumors. The Examiner's position is that various types of cancers have different causative agents and that one would not expect the compositions of this invention to be effective against all tumors; one of ordinary skill in the art could not use the entire scope of the claimed invention without undue experimentation.

Without acquiescing to the correctness of the Examiner's rejection, Applicants have amended claim 19 to delete reference to the "prevention" of tumors and replace it with "inhibition" of tumors. Support for this amendment appears in the specification at pages 15-16 and the Example 11 at page 42. This amendment is believed to obviate the Examiners rejection.

Applicants have also amended claim 21 to remove the reference to "a preventive measure" and to recite that the claimed method is used to inhibit the progression and growth of tumors after surgical excision. Support for this amendment appears in the specification at pages 15-16 and 42. Because no other

substantive rejections have been made against claims 19-22, Applicants respectfully request that this rejection be withdrawn and that claims 19-22 be allowed.

### III. 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner has rejected claims 19-22 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner has indicated that claim 19 is unclear because it lists an element "(a)" but fails to list an element "(b)." Applicants have amended claim 19 to remove the reference "(a)," and respectfully request that this rejection be withdrawn.

### IV. 35 U.S.C. § 103(A)

#### A. SUMMARY

Each of the Examiner's obviousness rejections discussed below combines references that teach or disclose a form of noscapine with references that teach or disclose a form of a controlled release mechanism. However, each rejection fails to include any reference that suggests that *noscapine* can be delivered to treat *neoplastic diseases*, as invented and presently claimed by Applicants. Thus, even if the references cited are properly combinable, which Applicants dispute, they do not teach the claimed invention.

In order to establish a *prima facie* case of obviousness, all claim limitations must be taught or suggested by the prior art. See *In re Ryka*, 490 F.2d 981 (CCPA 1974) (emphasis added). Because the use of noscapine in any delivery system to treat *neoplastic diseases* is not taught or suggested by these references, none of the references cited by the Examiner render the claimed invention obvious. In order to be fully responsive, Applicants nonetheless address each combination of references.

**B. AL-YAHYA ET AL. IN VIEW OF HYON ET AL.**

The Examiner has rejected claims 1-18 under 35 U.S.C. § 103(a) as being unpatentable over Al-Yahya et al. in view of Hyon et al. (U.S. Patent No. 5,100,669). The Examiner asserts that Al-Yahya teaches that noscapine is an alkaloid and that Hyon teaches administration of various types of pharmaceuticals, namely anti-cancer agents, in a drug delivery system that is release-controlled with polylactic acid type microspheres. The Examiner further states:

It is well known in the art that many alkaloids, such as noscapine, possess pharmacological activities. The determination of specific dosages, modes of administration as well as suitable excipients is well within the purview of one of ordinary skill in the art to prepare a noscapine derivative in a suitable delivery preparation along with pharmaceutically acceptable salts and excipients.

Applicants traverse this rejection and request reconsideration and withdrawal thereof.

Applicants respectfully submit that the references are not properly combinable. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *See In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 327 (Fed. Cir. 1992).

The Al-Yahya reference includes a description of the physical properties, preparation, biosynthesis, metabolism, and methods of analysis for noscapine. It does not, however, disclose the use or delivery of noscapine to treat neoplastic disease. In other words, the Al-Yahya reference does not suggest that noscapine is an anticancer drug.

The Hyon reference discloses polylactic microspheres for delivering a water soluble physiologically active substance and suggests that its particles can be used to deliver anticancer drugs. However, Hyon does not suggest or disclose the use or delivery of noscapine as an anticancer drug.

The cited references are directed to different fields of endeavor and to solving different problems. Accordingly, one of ordinary skill in the art would not have been motivated to combine the noscapine described by the Al-Yahya reference with the particles of the Hyon reference and expect to be able deliver the composition to treat neoplastic disease absent impermissible hindsight.

Moreover, even if the reference were properly combinable, the references do not teach or suggest the delivery of *noscapine* to treat *neoplastic disease* via a *controlled release mechanism*. As set forth above, in order to establish a *prima facie* case of obviousness, all claim limitations must be taught or suggested by the prior art. See *In re Ryka*, 490 F.2d 981 (CCPA 1974). Because noscapine used in a delivery system to treat *neoplastic diseases* is not taught or suggested by these references, they do not render the claimed invention obvious.

#### C. AL-YAHYA ET AL. IN VIEW OF BAR-SHALOM ET AL.

The Examiner has also rejected claims 1-18 under 35 U.S.C. § 103(a) as being unpatentable over Al-Yahya et al. in view of Bar-Shalom et al. (U.S. Patent No. 5,213,808). The Examiner characterizes Al-Yahya as described above, and Applicants incorporate the arguments submitted above herein by this reference. The Examiner further asserts that Bar-Shalom teaches the delivery of active-substances, which include anticancer agents, via the controlled-release of the pharmaceutically

active substances with a polymer matrix. The Examiner's position is that it would have been obvious to deliver a pharmaceutically active substance, such as noscapine, to an individual in need of a controlled-release delivery system, such as that taught by Bar-Shalom. Applicants respectfully traverse this rejection and request that it be withdrawn.

For reasons similar to those described in section IV (B) above, Applicants respectfully submit that the references are not properly combinable. The Al-Yahya reference does not disclose the use or delivery of noscapine to treat neoplastic disease or that noscapine is an anticancer drug. The Bar-Shalom reference discloses controlled pulsatile release articles for delivering active substances and suggests that one active substance may be anticancer agents. However, Bar-Shalom does not suggest or disclose the use or delivery of noscapine as an anticancer agent. One of ordinary skill in the art would not have been motivated to combine the noscapine described by the Al-Yahya reference with the article of the Bar-Shalom reference and expect to deliver the composition to treat neoplastic disease.

Moreover, even if the reference were properly combinable, the references do not teach or suggest the delivery of *noscapine* to treat *neoplastic disease* via a *controlled release mechanism*. Because noscapine used in a delivery system to treat *neoplastic diseases* is not taught or suggested by these references, they do not render the claimed invention obvious.

#### D. SAM ET AL. IN VIEW OF HYON ET AL.

The Examiner has further rejected claims 1-18 under 35 U.S.C. § 103(a) as being unpatentable over Sam et al. in view of Hyon et al. (U.S. Patent No. 5,100,669).

The Examiner asserts that Sam et al. teach that the opium alkaloid noscapine possesses none of the undesirable effects of narcotics, and it does possess various pharmacological properties, such as central nervous system activity and bronchodilation activity. The Examiner also characterizes the Hyon reference as described above. Applicants incorporate the arguments submitted above herein by this reference.

The Examiner asserts that the skilled artisan would have been motivated to employ the delivery system of Hyon et al. in order to administer the pharmaceutical of noscapine in a controlled release form as taught by Sam et al. Applicants respectfully traverse this rejection and request reconsideration and withdrawal thereof.

For reasons similar to those outlined above, the references are not properly combinable. The Sam reference does not disclose the use or delivery of noscapine to treat neoplastic disease or that noscapine is an anticancer drug. The Hyon reference discloses polylactic microspheres for delivering a water soluble physiologically active substance and suggests that its particles can be used to deliver anticancer drugs. However, it does not suggest or disclose the use or delivery of noscapine as an anticancer drug. As such, one of ordinary skill in the art would not have been motivated to combine the noscapine described by the Sam reference with the particles of the Hyon reference and expect to deliver the composition to treat neoplastic disease.

Additionally, even if the reference were properly combinable, the references do not teach or suggest the delivery of *noscapine* to treat *neoplastic disease* via a

*controlled release mechanism*, and as such, these references do not render the claimed invention obvious.

**E. SAM ET AL. IN VIEW OF BAR-SHALOM ET AL.**

The Examiner has also rejected claims 1-18 under 35 U.S.C. § 103(a) as being unpatentable over Sam et al. in view of Bar-Shalom et al. (U.S. Patent No. 5,213,808). The Examiner characterizes Sam et al. as described above, and Applicants incorporate the arguments submitted above herein by this reference. The Examiner also characterizes Bar-Shalom et al. as described above, and the above arguments and also incorporated herein by this reference.

The Examiner's position is that it would have been obvious to use the teachings of Bar-Shalom to administer or deliver a pharmaceutically active substance of noscapine to an individual and that the determination of specific dosages, modes of administration as well as suitable excipients is well within the purview of one of ordinary skill in the art. Applicants respectfully traverse this rejection and request reconsideration and withdrawal thereof.

For reasons similar to those described above, Applicants respectfully submit that the references are not properly combinable. The Sam reference does not disclose the use or delivery of noscapine to treat neoplastic disease or that noscapine can be used as an anticancer drug. The Bar-Shalom reference discloses controlled pulsatile release articles for delivering active substances and although it suggests that one active substance may be anticancer agents, it does not suggest or disclose the use or delivery of noscapine as an anticancer agent. As such, one of ordinary skill in the art would not have been motivated to combine the noscapine described by the Sam

reference with the article of the Bar-Shalom reference and expect to deliver the composition to treat neoplastic disease.

Again, even if the reference were properly combinable, they do not teach or suggest the delivery of *noscapine* to treat *neoplastic disease* via a *controlled release mechanism*. Because noscapine used in a delivery system to treat *neoplastic diseases* is not taught or suggested by these references, they do not render the claimed invention obvious.

### CONCLUSION

For at least the above reasons, Applicants respectfully request allowance of claims 1-22 and issuance of a patent containing these claims in due course. Applicants believe that no fees are due, but if mistaken, please charge any additional fees or credit any overpayment to Deposit Order Account No. 11-0855.

Respectfully submitted,

  
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